Understanding the Formaldehyde Science and Putting the Puzzle Pieces Together – Integrating New Science into Risk Evaluation Processes

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Hazard Characterization

Conclusions regarding formaldehyde carcinogenicity

- Regulatory Conclusions inconsistencies between EPA, ECHA, WHO, IARC, and NTP regarding the potential carcinogenicity of formaldehyde
- Diseases of Concern nasopharygeal (NPC) and all lymphohematopoietic (LHP) cancers
 - Some focus by selected agencies on the specific diseases - Acute Myeloid Leukemia (AML)
- NPC specific questions the potential for a threshold and rarity of the tumor
- LHP specific questions the biological plausibility of formaldehyde exposure causing all LHP cancers versus specific subtypes

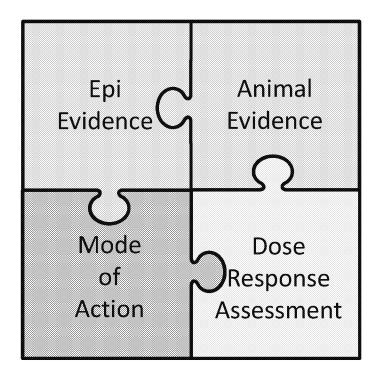
Hazard Characterization

Conclusions regarding formaldehyde carcinogenicity

Approaches to discuss:

- Systematic Review protocol development, evidence identification, evidence evaluation, analytic summary of the evidence
- Weight of Evidence a summary, considering both the quality and quantity of data to support conclusions regarding human carcinogenic potential
- Evidence Integration qualitative or quantitative approaches to integrate multiple streams of evidence to reach determinations of whether or not the evidence is adequate to draw conclusions related to potential hazard and causality
- Mode of action (MOA) frameworks evaluation of the available mechanistic or mode of action data in a systematic way to determine which proposed MOAs are supported by the available evidence and support causality and relevance to humans

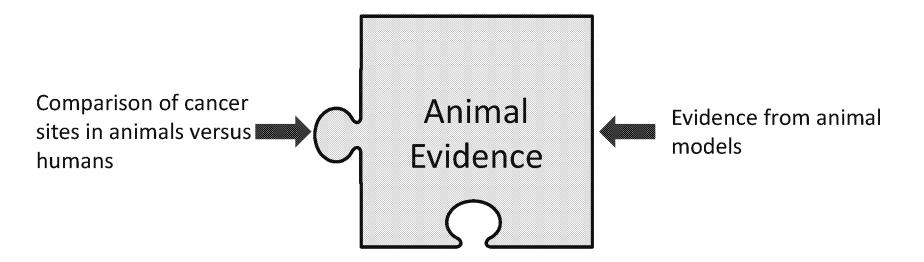
Integration of Evidence and Determination of Causality



NPC - Epidemiological

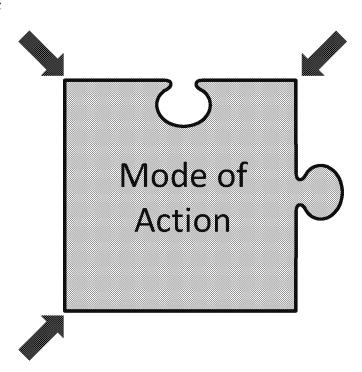
Defining the strengths, weaknesses, Evidence of upper respiratory and inconsistencies of key studies cancer versus other sites Selection of studies for Statistical power of studies, given rarity of cancer dose-response modeling

NPC - Animal



NPC - Mode of Action

Understanding the role of endogenous formaldehyde

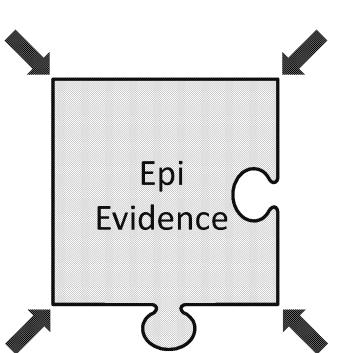


Role of mutagenicity and cytotoxicity

Potential for a threshold

LHP - Epidemiological

Specific versus grouped LHM cancers

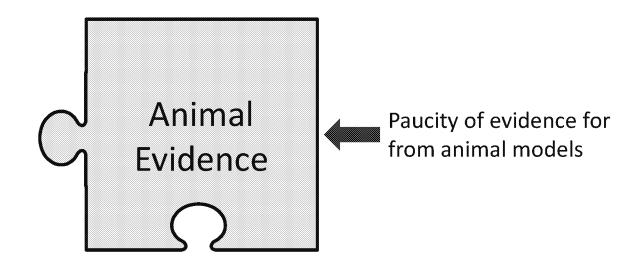


Defining the strengths, weaknesses, and inconsistencies of key studies

Understanding non-traditional exposure metrics

Selection of studies for dose-response modeling

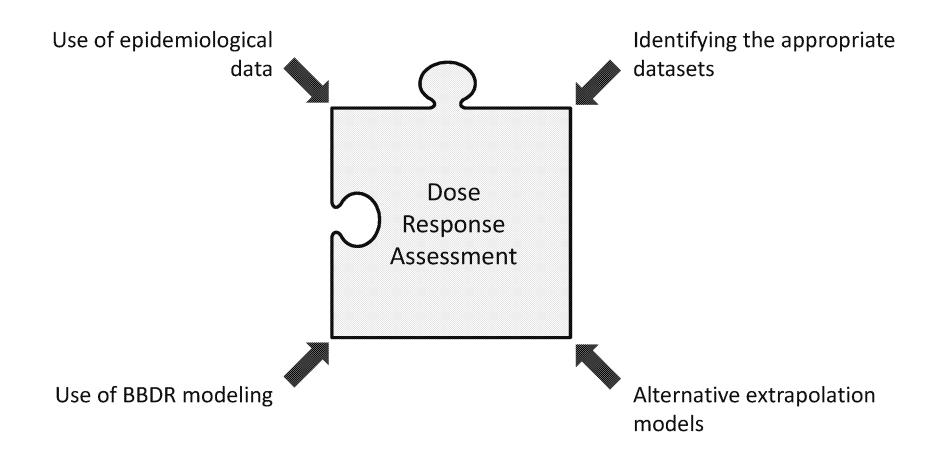
LHP - Animal



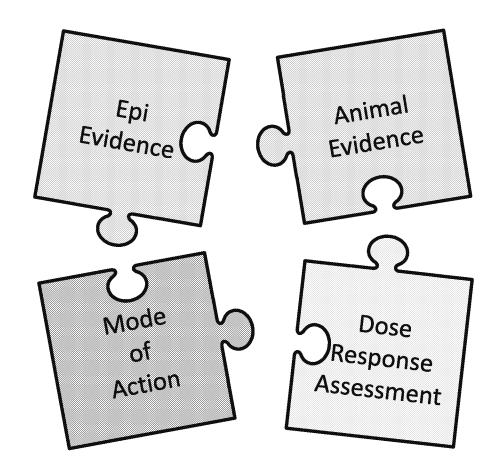
LHP - Mode of Action

Reconciling divergent Understanding the role of statements regarding endogenous formaldehyde systemic delivery Mode of Action Reconciling varying Data regarding potential for an euploidy/cytogenetic conclusions regarding effects at distant sites causality

Quantitative Analyses for Cancer



Putting the pieces together



How do we set up the framework for conducting a risk assessment for formaldehyde integrating the best available science and methods?